Transcriptional Regulation of Human Embryonic Stem Cells

Grant Award Details

Transcriptional Regulation of Human Embryonic Stem Cells

Grant Type: SEED Grant

Grant Number: RS1-00434

Investigator:

Name:	Miguel Ramalho-Santos
Institution:	University of California, San Francisco
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $595,755

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Transcriptional Regulation of Human Embryonic Stem Cells

Public Abstract:

Embryonic Stem (ES) cells can be grown indefinitely in the lab and can be turned into any cell type of the human body. Because of these properties, it may one day be possible to use ES cells to generate cell types in the lab that can then be transplanted into patients that need them. This approach may provide new treatments for devastating and presently incurable conditions such as type I diabetes, Parkinson's disease, muscular dystrophies, spinal cord injuries, and many others. However, before human ES cells can safely be used in the clinic, it will be essential to understand how they function. For example, if rapid cell division is not kept in check in ES cells, they can give rise to tumors upon transplantation. Our proposal is directly aimed at understanding the genetic regulation of human ES cells.

We developed a very innovative approach to understand how gene activity is regulated in human ES cells. Our very significant progress so far it can be summarized as follows:- we identified the genes that are preferentially activated in ES cells;- we discovered several DNA sequences that act as genetic switches to turn ES cell genes on or off;- we identified an operator protein that activates one of these switches;- we discovered that this protein is essential to maintain rapid cell division of mouse ES cells.We now propose to investigate the function of this protein in human ES cells. We further propose to identify other operator proteins that activate genetic switches revealed by our work. Our ultimate goal is to identify all the operator proteins, the corresponding genetic switches, and their combined mode of action in human ES cells.

We expect that this research will make the following significant contributions:1. Our research may lead to the development of diagnostic tests that detect the activity of the operator proteins and genetic switches that we have identified. These diagnostic tests may be important tools for quality control of human ES cells;2. The operator proteins identified are expected to be critical regulators of rapid cell division of human ES cells. Understanding what those operator proteins are may lead to the development of new drugs to prevent the formation of tumors upon transplantation of ES cells;3. The current methods to obtain a particular cell type from ES cells still result in a mixture of different cell types. If we understand how genes are activated in ES cells, we may be able to turn on the precise set of genes that leads to the formation of a particular cell type of interest, and thus obtain pure populations of cells needed by patients;4. If we understand what are the essential operator proteins that regulate gene activity in ES cells, we may be able to formulate a cocktail of these proteins that is capable of resetting the genetic program of a patient's own cells back to that of ES cells. This way the transplanted cells will be immune-matched to the patient, and therefore will not be rejected.

Statement of Benefit to California:

Human embryonic stem cells hold the potential to revolutionize medicine and health care. Research on human embryonic stem cells may provide new treatments for devastating and presently incurable conditions such as type I diabetes, Parkinson's disease, muscular dystrophies, spinal cord injuries, and more than 70 other diseases. We anticipate that our research will be a significant step towards making the promise of human embryonic stem cells a reality.

Our proposal aims to identify genes that regulate the properties of human embryonic stem cells. This research will pave the way for the development of safe clinical applications of human embryonic stem cells. If we understand the genetic mechanisms that regulate human embryonic stem cells, we will be able to manipulate those mechanisms so as to obtain cell types of therapeutic value, while avoiding unintended side-effects. The development of human embryonic stem cell-based therapies will significantly increase the options available in the California health care system. These new therapies are expected to reduce the long-term health care costs to California by providing cures to diseases that are currently chronic and require expensive periodic treatment.

Our research is also expected to stimulate the development of biotechnology industry focused on clinical applications of human embryonic stem cells. Such development will be of great benefit to California by attracting high-skill jobs and tax revenues, and by making the State a leader in a field that is poised to be the economic engine of the future. The State of California will also stand to benefit from the intellectual property generated by this research.

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